UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/049,696	03/27/98	BILLING-MEDEL	P 6067.US.01

EXAMINER	
ART UNIT	PAPER NUMBER
1633	13

HM22/0706

STEVEN F WEINSTOCK
ABBOTT LABORATORIES
D-377/AP6D
100 ABBOTT PARK ROAD
ABBOTT PARK IL 60064-3500

KERR, J

DATE MAILED: 07/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/049,696	Applicant(s) Billing-Medel et al.
	Examiner Janet M. Kerr	Group Art Unit 1633

☒ Responsive to communication(s) filed on *Apr 12, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-18* is/are pending in the application.

Of the above, claim(s) *7-10, 12-14, and 16* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 11, 15, 17, and 18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Response to Amendment

Applicants' amendment, filed 4/12/00, has been entered.

Claims 1-18 remain pending.

Claims 7-10, 12-14, and 16 had been withdrawn from consideration as being directed to a non-elected invention as set forth in the office action of 1/4/00, Paper No. 9.

Claims 1-6, 11, 15, 17, and 18 are being examined on the merits.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 11, 15, 17, and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either an asserted utility or a well established utility.

The claims are directed to purified polynucleotides selected from the group consisting of polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof, which can encode an epitope; recombinant expression systems comprising polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof; cells comprising polynucleotides encoding an epitope wherein the polynucleotides are selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof; a gene, or fragment thereof, which codes for a protein comprising an amino acid sequence that has at least 60% identity with SEQ ID NO. 41; a gene, or fragment thereof, comprising DNA having at least 50% identity with SEQ ID NO. 18, 19, or 20.

The disclosed utilities of the polynucleotides include assaying test samples for products of a GI tract tissue gene designated as CS194; assaying for translation products of CS194, providing

reagents such as oligonucleotide primers and peptides; producing encoded polypeptide sequences which are useful as standards or reagents in diagnostic immunoassays, as targets for pharmaceutical screening assays, and/or as components or as target sites for various therapies. Monoclonal and polyclonal antibodies directed against at least one epitope contained within these polypeptide sequences are useful as delivery agents for therapeutic agents as well as for diagnostic tests and for screening for disease or conditions associated with CS194, especially GI tract cancer; to isolate sequences of other portions of the gene of interest and use these sequences in detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, or determining the predisposition to diseases and conditions of the GI tract, such as GI tract cancer; for identification of certain markers as indicative of a GI tract tissue disease or condition (see e.g., pages 10, 11, 21, of the specification). The disclosed utilities of the polypeptides or fragments thereof of the invention include: to produce antibodies, and to use the peptides in an assay for the detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, or determining the predisposition to diseases and conditions of the GI tract, such as GI tract cancer (see, e.g., pages 10, 46, and 47 of the specification).

The specification discloses that the polynucleotides of the instant invention are partially homologous to a polynucleotide encoding a bovine chloride channel protein (see page 53, lines 11-14). However, the specification does not indicate the degree of homology to the bovine chloride channel, either with respect to the polynucleotide or polypeptide, or the structural features which render the polypeptide structural similar to the bovine chloride channel protein. In addition, the specification does not provide polynucleotide or polypeptide sequence comparisons, nor does the specification identify any common structural motifs associated with the disclosed polypeptides and which are contained in putative chloride channel polypeptides. Moreover, no biological activities have been established for the polypeptides encoded by the polynucleotide.

The specification does not provide evidence that any of the claimed polynucleotides having less than 100% identity to CS194 encode a chloride channel, one of skill in the art would not know the structure or function of the claimed polynucleotides, nor would one of skill in the

art know how to use the claimed invention, i.e., polynucleotides having at least 50%, 60%, or 70% identity, for the stated purpose without initial research to further characterize the products or information obtained when using the polynucleotide.

With regard to the utility of the polynucleotide as a probe for screening GI tract tissue as a diagnostic for cancer, it is noted that the expression of the protein is not limited to cancerous tissue, i.e., CS194 is also detected in normal GI tract tissue (see Figure 3 of the specification). Therefore, with regard to utilizing the CS194 polynucleotide, polypeptide, or antibodies derived therefrom as diagnostic reagents or as reagents in methods of treatment of GI cancer, and inasmuch as the function of the polypeptide is not known, further research would be required to assess the biological relevance of the expression of CS194 in the GI tract.

With regard to the utility of the polynucleotides for obtaining genomic clones, the specification does not disclose any genomic clones related to the claimed polynucleotides having at least 50%, 60%, or 70% identity to CS194, or how one would recognize that the obtained genomic clones, isolated by hybridization to the claimed polynucleotides having at least 50%, 60%, or 70% identity to CS194, were in fact related to CS194. Thus, further analysis and characterization of the isolated polynucleotides, as well as the products encoded by the polynucleotides would be required.

With regard to the utility of the polynucleotide to produce polypeptides for producing antibodies, or used as a diagnostic for the detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, or determining the predisposition to diseases and conditions of the GI tract, such as GI tract cancer, the utilization of the polynucleotide results in a product which requires further analysis and characterization; without such analysis and characterization, the potential therapeutic utility is unknown. Thus, with regard to using the polynucleotides to generate polypeptides, which are subsequently used in generating antibodies, the utility of such antibodies are not known as the specification has not taught any biological function of the protein. Thus, utilization of the polynucleotides, polypeptides, and products generated therefrom, as therapeutic tools, requires further research and characterization.

These recited utilities are merely hypothetical or general utilities for which the claimed invention might be used, once the necessary information is known.

Consequently, there is no immediate benefit to the public since the claimed invention must be further characterized to provide the information necessary for practicing these utilities. Such further characterization amounts to research on the claimed invention itself, a non-statutory utility, including use-testing, i.e., research aimed at finding a specific utility for the invention. Thus, for the claimed invention wherein the nucleic acid comprises less than the entire region of the recited nucleotide sequences coding for the signal sequence, the only apparent utility is for use-testing. *Brenner v. Manson*, 148 USPQ 689, 696 (US SupCt., 1966) noted that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.".

In view of the above discussion, one skilled in the art would not readily attribute chloride channel protein activity encoded by the claimed polynucleotides in view of the low sequence similarity and lack of sequence conservation therein. In view of such, it is not readily apparent that chloride channel protein activity could be attributed to the deduced amino acid sequence of the claimed polynucleotides. Therefore, the asserted uses for the claimed polynucleotides are not considered to be supported by either a specific and/or substantial utility, since no function can be ascribed to the gene, and since no specific disease state has been identified to be associated with the claimed gene.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 1-6, 11, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. See Interim guidelines for the requirement for Written Description as cited in the Federal Register, Vol. 63, No. 114, p. 3263.

The claims are directed to purified polynucleotides selected from the group consisting of polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof, which can encode an epitope; recombinant expression systems comprising polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof; cells comprising polynucleotides encoding an epitope wherein the polynucleotides are selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof; a gene, or fragment thereof, which codes for a protein comprising an amino acid sequence that has at least 60% identity with SEQ ID NO. 41; a gene, or fragment thereof, comprising DNA having at least 50% identity with SEQ ID NO. 18, 19, or 20. Claims 17 and 18 are directed to genes.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In this case, the nucleic acid sequences encoding CS194 as set forth in SEQ ID NOS. 1-20 are the only species whose complete structure is disclosed. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence). Possible identifying characteristics could include size of the polynucleotide, the location to which it maps in the genome, restriction maps, biological activity of the encoded product, etc. No such identifying characteristics are provided for any polynucleotide. While applicants were obviously in possession of the nucleic acid sequences as set forth in the disclosed SEQ ID NOS. 1-20 the

specification provides no information regarding other nucleic acid sequences having 50%, 60%, or 70% identity to SEQ ID NOS. 1-20. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of polynucleotides besides those set forth in SEQ ID NOS. 1-20, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

With regard to claims 17 and 18, directed to genes, in view of the fact that the art does not provide an accepted definition for the term "gene", an elaboration of its characteristics (i.e., sequence) would require both a disclosure of a definition for the term and a characterization of the sequence thereof. However, the specification does not provide a definition for the term, nor has the specification provided a description of the genomic DNA sequences encompassed by the claims as the instant polynucleotides only include the coding region of the gene(s) from which it is derived. Applicants have not adequately described the nature of the genomic DNA corresponding to SEQ ID NOS: 1-20 because no structural information has been provided for non-coding regions of the gene such as, for example, introns, promoters or ribosomal binding sites. Such structural information cannot be predicted based solely on a knowledge of the coding region. As the specification does not disclose that any nucleotide sequences beyond that of the corresponding DNA of the coding region exist, one skilled in the art would not recognize that applicants had possession of polynucleotide sequences other than those only set forth in SEQ ID NOS. 1-20 at the time of filing.

With regard to polynucleotides encoding epitopes wherein the polynucleotides have 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, or 70% identity to SEQ ID NOS. 9, 13, and 14, or complements thereof, the specification fails to disclose any particular sequence having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, or 70% identity to SEQ ID NOS. 9, 13, and 14, or complements thereof. The information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of polynucleotides

encoding epitopes, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed polynucleotides encoding epitopes.

Enablement

Claims 1-6, 11, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to purified polynucleotides selected from the group consisting of polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof, which can encode an epitope; recombinant expression systems comprising polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof; cells comprising polynucleotides encoding an epitope wherein the polynucleotides are selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof; a gene, or fragment thereof, which codes for a protein comprising an amino acid sequence that has at least 60% identity with SEQ ID NO. 41; a gene, or fragment thereof, comprising DNA having at least 50% identity with SEQ ID NO. 18, 19, or 20. Claims 17 and 18 are directed to genes.

The instant specification is directed to the preparation and sequence characterization of particular polynucleotides that are disclosed. The claimed SEQ ID NOS. represent fragments or overlapping sequences of cDNA clones prepared using the methods disclosed in the specification. However, these are the only polynucleotides whose sequences are disclosed. The specification does not disclose a CS194 gene *per se*, nor does the specification provide an example of the genomic structure of CS194, nor methods, including the necessary reagents, which would be used to specifically isolate the gene. In view of the lack of an example of the genomic structure of the CS194 gene, or sequences comprising 5' regulatory regions or intronic regions of the CS194

gene, and in view of the lack of guidance as to the methods and reagents required for isolating the gene, one of ordinary skill in the art would not have had a high expectation of successfully isolating a CS194 gene without undue experimentation. Moreover, the claims are directed to polynucleotides which have 50%, 60% or 70% identity with the claimed polynucleotides. However, the specification does not provide the sequences associated with these claimed polynucleotides; one of skill in the art would not know the structure of such polynucleotides, or how to use polynucleotides of unknown structure. Therefore, given that the specification fails to teach how one would prepare the disclosed sequences that would be useful for any particular function with any particular specificity, the artisan would be required to exercise undue experimentation in the preparation and use of the claimed polynucleotides.

It should be noted that the specification does not teach a specific algorithm or parameters required to calculate the claimed sequence identity. For example, the necessary parameters required to calculate the claimed sequence identity, using a disclosed, given algorithm, include gap penalties and mismatch penalties. As percent identity may vary depending upon how gaps, substitutions, and sequences of unequal length are scored, one of ordinary skill in the art would not have been able to make any particular DNA sequence at less than 100% identity without undue experimentation.

With regard to claims 4 and 11, which are directed to polynucleotides encoding an epitope wherein the polynucleotides are selected from polynucleotides having 50% identity to SEQ ID NOS. 1-8, 10-12, 15-20, and polynucleotides having 70% identity to SEQ ID NOS. 9, 13 and 14, or complements thereof; or cells comprising polynucleotides encoding an epitope wherein the polynucleotides are selected from the group consisting of SEQ ID NOS. 1-20, and fragments or complements thereof, the specification does not provide any examples of polynucleotides having 50% or 70% identity to the SEQ ID NOS., nor any epitopes which may be encoded by these SEQ ID NOS., nor does the specification provide specific guidance as to how to select appropriate fragments of SEQ ID NOS. 1-20 which encode an epitope. The specification does not provide guidance as to how one of skill in the art would select an appropriate polynucleotide sequence

encoding an amino acid sequence which functions as an epitope. Moreover, while the specification discloses that the nucleotide sequences contain open reading frames from which an immunogenic epitope may be found, and that such an epitope is believed to be unique to the disease state or condition associated with CS194, the specification does not disclose any epitope which is unique to a disease state or condition associated with CS194. Thus, absent examples of specific epitopes which are unique to a disease state or condition associated with CS194, and in view of the lack of guidance in the specification as to how to select the nucleic acid sequences which would encode such suitable epitopes, one of skill in the art would not have had a high expectation of successfully and reproducibly determining the appropriate nucleic acid sequences to use in generating CS194 epitopes without undue experimentation.

Taken together, the claims are not enabled because of the large number of sequences embraced by the claims coupled with the lack of adequate guidance in the application as to which sequences to isolate or construct, and how to use such sequences such that use of such sequences does not require further experimentation. Thus, one of skill in the art would need to perform undue experimentation to practice the claimed invention. The Court of Appeals for the Federal Circuit has ruled that claims that embrace a large number of species of polynucleotide sequences without proper guidance in the application as to how to make and use such polynucleotides do not meet the requirements of 35 U.S.C. § 112, first paragraph, *Amgen v. Chugai* (18 USPQ2d 1016 (Fed. Cir. 1991)).

Applicant's arguments with respect to claims 1-6, 11, 15, 17, and 18 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 remains rejected under 35 U.S.C. 102(b) as being anticipated by Cunningham *et al.* (J. Biol. Chem., 270:52, 31016-31026, 1995) for the reasons of record and the reasons below.

Cunningham *et al.* disclose isolated polynucleotides which have at least 50% identity with SEQ ID No. 18 as follows (see Figure 1 on pages 31018-31019 of the reference and also the attached nucleic acid comparison results):

SEQ ID NO.	Location in Reference	Location in Prior Art SEQ	Location in claimed SEQ ID NO.
SEQ ID NO 18	"origin"	7-2637	13-2625
SEQ ID NO 19	"origin"	1304-2637	1-1325
SEQ ID NO 20	"origin"	7-2637	13-2625

As the polynucleotide of Cunningham *et al.* has at least 50% identity with SEQ ID No. 18, the polynucleotide sequence of Cunningham *et al.* anticipates the claimed invention.

Applicant's arguments filed 4/12/00 have been fully considered but they are not persuasive. Applicants argue that the rejection is moot in view of applicants' amendment directed to deleting the term "fragment" in the claims (see applicants' Response, page 5). This is not persuasive as

there is no indication in applicants' amendment to delete the phrase "fragment thereof" in claim 18.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to John LeGuyader, Supervisory Primary Examiner, at (703) 308-0447. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Janet M. Kerr, Ph.D.
Patent Examiner
Group 1600

JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JOHN L. LeG
SUPERVISORY PAT
TECHNOLOGY C